POSTHERPETIC OPHTHALMIC NEURALGIA

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ABSTRACT

Postherpetic ophthalmic neuralgia is the final stage of a varicella zoster infection. Many years after chickenpox infection, patients can develop herpes zoster in one or more specific dermatomal regions. The ophthalmic branch of the trigeminal nerve and the thoracic nerves are most commonly affected. Younger patients are less prone to postherpetic neuralgia than the older. Patients with a depression in cell-mediated immunity are more susceptible to develop postherpetic pain. Postherpetic ophthalmic neuralgia is a neuropathic pain and can be treated by anticonvulsants and tricyclic antidepressants. Neurodestructive procedures are not recommended as they enhance destruction and neuropathic pain. Sympathetic nerve blocks can be helpful. Neurostimulation is the last therapeutic resort.

RÉSUMÉ

La névralgie postzostérienne ophtalmique est la conséquence d'un zona dans le territoire de la branche ophtalmique du trijumeau. La réactivation du virus de la varicelle résulte le plus souvent d'une maladie de la peau dans la région. Des vésicules apparaissent intialement, suivies de croûtes et enfin de cicatrices. Les personnes âgées et les patients immunodéprimés ont plus de chances de présenter des douleurs neuropathiques par la suite. Les patients se plaignent de paresthésies, d'élancements ou d'allodynie. Les douleurs peuvent être traitées par des anticonvulsifs, des antidépresseurs ou des infiltrations des nerfs. La destruction du trijumeau n'est plus pratiquée. Si la douleur ne réagit pas au traitement médicamenteux ou aux infiltrations, la stimulation cérébrale (thalamus ou cortex moteur) reste comme dernière option thérapeutique.

SAMENVATTING

Postherpetische neuralgie in de oftalmische tak van de aangezichtszenuw is het eindstadium van een varicella zoster infectie.
Jaren na het doormaken van een varicella zoster besmetting kunnen patiënten een herpes zoster eruptie ontwikkelen in één of meerdere lichaamsdermatomen. De oftalmische tak van de trigeminuszenuw is hier vaak in betrokken. Oudere patiënten met een cel-gemedieerde immuniteitsdaling zijn hiervoor gevoeliger dan jonge patiënten. Zona ophthalmica kan vaak aanleiding geven tot neuropatische pijn die afneemt met anticonvulsiva en tricyclische antidepressiva. Neurodestructieve behandelingen zijn te ontraden omdat zij neuropathische pijn in de hand werken. Zenuwinfiltraties, zowel lokaal als ter hoogte van de cervicale sympatische vezels, kunnen pijnverlichting geven. Neurostimulatie is soms de laatste therapeutische oplossing.

KEY-WORDS

neuropathic pain, zoster infection, co-analgesics, nerve blocks, nerve stimulation.

MOTS-CLÉS

maladie postzostérienne, douleur neuropathique, infiltration, stimulation cérébrale.

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INTRODUCTION

Postherpetic neuralgia is the consequence of a herpes zoster infection. The latter results in the reactivation of a primary varicella infection in childhood. Chickenpox is the disease of childhood, while the herpes zoster incidence increases sharply in the elder population, doubling in each decade past the age of 50 years. Herpes zoster is infrequent in the young population less than 15 years. On the contrary, patients older than 50 years account for more than 30 percent of the zoster infections(4).
Not only herpes zoster incidence is increasing by age but symptoms also become more severe. Postherpetic neuralgia is defined as neuropathic pain persisting more than 3 months after herpes eruption(15).

HERPES ZOSTER INFECTION

As mentioned in the introduction, herpes zoster occurs mainly in the elder population. This age related increase could be explained by a decrease in cell-mediated immunity by which reactivation of the varicella zoster virus reactivation occurs(2). Patients with other diseases affecting cell-mediated immunity, such as human immunodeficiency virus infection (HIV) or with malignancies such as Hodgkin's lymphoma, are more prone to develop herpes zoster infections(28). Patients receiving radiotherapy, chemotherapy or corticoid therapy also have a higher herpes zoster incidence than the normal population.
Differences in race are also noticed. Blacks are one fourth as likely as whites to develop herpes zoster infections. This difference can not immediately be explained(27).

PATHOPHYSIOLOGY OF HERPES ZOSTER

Chickenpox or the primary varicella zoster infection is the primary infection in childhood. During that period the virus provokes a generalized disease with cutaneous lesions over the whole body entering the sensory dorsal root ganglia(15). After this acute disease, the virus remains latent for decades into the ganglia as the varicella genome has been identified in the trigeminal ganglia of nearly all seropositive patients. Reactivation of the virus occurs following a decrease in virus-specific cell-mediated immunity(7,14). The reactivated virus travels down the sensory nerve and is the cause for the dermatomal distribution of pain and skin lesions. Most infections are noticed in the Dorsal 5 and 6 dermatomal region and the ophthalmic branch of the trigeminal nerve (24). A maculopapular rash followed by crust formation is noticed at the skin. Finally after one to several weeks, only scars remain at the affected dermatomes.
Herpes zoster can already have prodromal signs such as burning pain, paresthesias or pruritus, preceeding the skin eruption. Sometimes, a burning or stinging pain is the only dominant symptom during the zoster infection and skin lesions can be limited. However, ocular complications such as conjunctivitis, episcleritis, keratitis and anterior uveitis can occur in approximately one half of the patients with involvement of the ophthalmic division of the trigeminal nerve. Normally, pain recedes after skin healing but postherpetic pain can persist especially in the elder population. So, it has been demonstrated that if patients receive antiviral agents within 72 hours after the onset of the rash, the duration of herpes zoster rash and the severity of the pain can be decreased. The chance to develop postherpetic zoster pain is also smaller in patients receiving antiviral therapy in the prodromal phase of a zoster eruption(9,29).
Acyclovir is the prototype antiviral drug and can be administered orally or intravenously(10).
Corticosteroids can also be administered in the treatment of herpes zoster to decrease the degree of neuritis caused by active infection. Some studies demonstrated some benefit in the prevention of postherpetic neuralgia, while others could not. Corticosteroids are also administered in the treatment of ocular herpes zoster infection(1,11-13,17).
In the acute phase of the zoster infection, lancinating or burning pain can already be present. Anticonvulsants are used to treat the lancinating pain while the tricyclic antidepressive drugs are prescribed for the burning pain(13,16).

POSTHERPETIC NEURALGIA

Postherpetic neuralgia can be defined as neuropathic pain persisting more than 3 months after scar tissue formation. Normally pain should be limited in function of time. Unfortunately, 25% of the patients are complaining of pain six months after skin eruption and 5% of the patients notice pain more than one year after eruption.

Lancinating pain and paresthesias sometimes associated with allodynia (pain after repeated non noxious stimuli such as washing the face or brushing the hair) is noticed in postherpetic ophthalmic neuralgia. As postherpetic ophthalmic pain can be very severe, even disturbing sleep and disabling patients, it should be prevented as well as possible. Especially in the older patients acute herpes zoster infection should be treated with antiviral agents and corticosteroids(14).

Once the postherpetic neuralgia syndrome has settled, tricyclic antidepressants can effectively reduce dysesthesias and/or allodynia(18,23). These agents probably reduce pain by inhibiting the re-uptake of serotonin and norepinephrine neurotransmitters in the brain and spinal cord enhancing central pain inhibitory pathways. However, despite the low dose, tricyclic antidepressants can induce some side-effects as sedation, dry mouth, hypotension and urinary retention; narrow-angle glaucoma is a contra-indication. Amitriptyline is frequently used in a dose of 25-50 mg daily. Its analgesic effects must appear within the first week.

Anticonvulsants such as carbamazepine (Tegretol®), sodiumvalproate (Depakine®), gabapentin (Neurontin®) and lamotrigine (Lamictal®) are often used to control the lancinating pain and allodynia(19,25). Analgesic dosages are often lower than those used in epilepsy treatment and depression. Drug treatment can be limited by side effects such as: sedation, memory disturbances, liver toxicity and trombocytopenia.

Anticonvulsants act by blocking sensory nerve voltage gated sodium channels or calcium channels(3). Some anticonvulsants also block some NMDA receptors reducing sensitization and allodynia. As trigeminal neuropathic pain can be mediated by activation of sodium channels local anesthetics and some anti-arhythmic drugs as mexilitine can be effective in the treatment of postherpetic ophthalmic neuralgia(16). If drug treatment is ineffective despite adequate dosage, nerve infiltration with local anesthesia can be tried(6,31). Sometimes prolonged and sustained analgesia has been reported. Nerve destruction should be prevented as postherpetic neuralgia is already the consequence of nerve tissue damage(30).

In many patients, neuropathic pain is maintained by sympathetic function(8,26,31). This is also been noticed in postherpetic ophthalmic neuralgia. So, infiltration at the stellate ganglion or the sphenopalatinum ganglion with local anesthetics can be beneficial and sustained analgesia can be obtained after repeated sympathetic blocks. Although postherpetic neuralgia should be selflimiting in time, it can persist for many years, severely disabling patients. If none of the above mentioned treatments are effective, neuromodulation can be tried(21). Transcutaneous electrical nerve stimulation is an option but applying electrodes in the face is very uncomfortable. So, deep brain stimulation into the thalamus nuclei, eliciting pain relieving paresthesias in the ophthalmic region, is a much more invasive technique(22). Nevertheless, 50% of the patients can obtain sufficient pain relief by this treatment. Electrical motor cortex stimulation, with electrodes applied at the pregyral sulcus is a little less invasive neurosurgical procedure to produce analgesia for neuropathic pain in the ophthalmic region. Electrical stimulation is applied at subthreshold levels not eliciting motor response nor paresthesias. Nevertheless, pain relief can be induced. If the stimulation threshold is too high, motor response can be evoked and convulsions can be elicited(20). Obviously, motor cortex stimulation or deep brain stimulation are last resort therapies for postherpetic ophthalmic neuralgia.

CONCLUSION

Although postherpetic ophthalmic neuralgia is only the result of the varicella zoster virus reactivition in the ophthalmic branch of the trigeminal nerve, it can end in severe nerve destruction leading to ophthalmic complications with

loss of vision and longstanding pain. Prevention of postherpetic neuralgia in the elderly is essential. Once postherpetic ophthalmic neuralgia has installed, anticonvulsants, tricyclic antidepressants and nerve blocks can be used. Brain neurostimulation is exceptional and a far more invasive treatment option.

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